Synthesis of Bis-Heterocyclic 1H-Imidazole 3-Oxides from 3-Oxido-1H-imidazole-4-carbohydrazides

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Abstract: The reaction of 1H-imidazole-4-carbohydrazides 1, which are conveniently accessible by treatment of the corresponding esters with NH2NH2 · H2O, with isothiocyanates in refluxing EtOH led to thiosemicarbazides (= hydrazinecarbothioamides) 4 in high yields (Scheme 2). Whereas 4 in boiling aqueous NaOH yielded 2,4-dihydro-3H-1,2,4-triazole-3-thiones 5, the reaction in concentrated H2SO4 at room temperature gave 1,3,4-thiadiazol-2-amines 6. Similarly, the reaction of 1 with butyl isocyanate led to semicarbazides 7, which, under basic conditions, undergo cyclization to give 2,4-dihydro-3H-1,2,4-triazol-3-ones 8 (Scheme 3). Treatment of 1 with Ac2O yielded the diacylhydrazine derivatives 9 exclusively, and the alternative isomerization of 1 to imidazol-2-ones was not observed (Scheme 4). It is important to note that, in all these transformations, the imidazole N-oxide residue is retained. Furthermore, it was shown that imidazole N-oxides bearing a 1,2,4-triazole-3-thione or 1,3,4-thiadiazol-2-amine moiety undergo the S-transfer reaction to give bis-heterocyclic 1H-imidazole-2-thiones 11 by treatment with 2,2,4,4-tetramethylcyclobutane-1,3-dithione (Scheme 5).

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3-Oxidoimidazole-4-carbohydrazides for the Synthesis of some Bis-heterocyclic Imidazole *N*-Oxides

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The reaction of 1*H*-imidazole-4-carbohydrazides **1**, which are conveniently accessible by treatment of the corresponding esters with $NH_2NH_2 \cdot H_2O$, with isothiocyanates in refluxing EtOH led to thiosemicarbazides **4** in high yields (*Scheme 2*). Whereas **4** in boiling aqueous NaOH yielded 1,2,4-triazole-5-thiones **5**, the reaction in conc. H_2SO_4 at room temperature gave 5-amino-1,3,4-thiadiazoles **6**. Similarly, the reaction of **1** with butylisocyanate led to semicarbazides **7**, which under basic conditions cyclized to give 1,2,4-triazol-5-ones **3** (*Scheme 3*). Treatment of **1** with Ac_2O yielded the diacylhydrazines **9** exclusively, and the alternative isomerization of **1** to imidazol-2-ones was not observed (*Scheme 4*). It is important to note that in all these transformations the imidazole *N*-oxide residue is retained. Furthermore, it was shown that imidazole *N*-oxides bearing a 1,2,4-triazole-5-thione or 5-amino-1,3,4-thiadiazole substituent undergo the S-transfer reaction to give bis-heterocyclic imidazole-2-thiones **11** by treatment with 2,2,4,4-tetramethylcyclobutane-1,3-dithione (*Scheme 5*).

1. Introduction. - Acid hydrazides (carbohydrazides) and the corresponding hydrazones are well known as a class of compounds with diverse biological activities [1]. Particularly important are derivatives bearing a heterocycle, and one of the best-known examples is isoniazid (isonicotinohydrazide) [2]. Imidazole derived hydrazides were also reported to display biological activity [3], and the majority of reports remain to patents (*e.g.*, ref. [4]). However, in most cases, *N,N*-disubstituted hydrazides were described, which are of limited interest with respect to their use as building blocks for new heterocyclic systems.

The *N*-unsubstituted carbohydrazides are widely applied as unique building blocks for the synthesis of diverse five- and six-membered heterocycles such as pyrroles, pyrazoles, thiazolidines, 1,2,4-triazoles, phthalazines, pyrimidines, etc. [5]. A typical procedure for the preparation of unsubstituted hydrazides is the treatment of the corresponding carboxylic ester with $NH_2NH_2 \cdot H_2O$ [1][5]. In a recent publication we have reported on the application of this method for the preparation of diverse types of unsubstituted hydrazides containing in their structure the imidazole ring [6]. The precursors of 4-imidazoyl hydrazides **1** were the esters **2**, available *via* condensation of ethyl 2-hydroxyimino-3-oxobutanoate (**3**), a primary amine, and formaldehyde [7] (*Scheme 1*).

Scheme 1

In earlier papers, we presented the synthetic potential of the 'nitrone-like' fragment of 2-unsubstituted imidazole *N*-oxides [8]. The goal of the present study was the synthesis of new bis-heterocycles with the preserved imidazole *N*-oxide unit by exploration of the reactivity of the carbohydrazido group in compounds **1**. In

preliminary experiments it was shown that hydrazides **1** can be used for the preparation of bis-heterocycles [6]. To the best of our knowledge, there are no other bis-heterocycles with the reactive *N*-oxide function known to date (cf. [6]).

Results and Discussion. – As described earlier, imidazole *N*-oxides **1** with the hydrazido substituent of C(4) are stable, colorless, crystalline materials [6]. In contrast to the corresponding esters they did not undergo the thermal isomerization to imidazol-2-ones. Even more surprisingly, they could neither be converted to the corresponding imidazole-2-thiones *via* the 'sulfur-transfer reaction' [8a] nor reduced to the parent system by treatment with *Raney*-Ni [8c].

It seems likely that these diminished reactivity of the N→O function is the result of a strong intramolecular H-bond [6][8d]. On the other hand, reactions with aldehydes and aliphatic ketones occurred smoothly yielding the expected hydrazones [6]. In addition, a preliminary experiment showed that thiosemicarbazide **4a** obtained from **1a** (R = $PhCH_2$) and methyl isothiocyanate underwent the cyclocondensation yielding, depending on the reaction conditions, bis-heterocycles **5a** or **6a**. In analogy to **1a**, derivatives **1b** and **1c** were also reacted with other isothiocyanates (R^2 = Bu, Ph), and the thiosemicarbazides **4** were heated in a 2% aqueous solution of NaOH to give the triazole-3-thiones **5** (*Scheme 2*). In addition, the sterically crowded *tert*-butylisothiocyanate was used for the reaction with **1a**, and the expected thiosemicarbazide **4d** was obtained in good yield as a crystalline material. However, the attempted cyclization of **4d** under basic conditions was unsuccessful and the starting material was recovered in nearly quantitative yield. Apparently, in this case, steric hindrance resulting from the presence of the bulky *tert*-butyl group at the N-atom does not allow the system to undergo the cyclization.

Scheme 2

The structure of the triazole-3-thiones **5** was indicated by the C=S absorption in the ^{13}C-NMR spectra at 168 – 169 ppm. In addition, the unchanged *N*-oxide structure of the imidazole was confirmed by the characteristic ^{1}H-NMR absorption of H–C(2) at 8.6 – 8.1 ppm.

The alternative course of the cyclocondensation was observed when thiosemicarbazides of type **4** were stirred in conc. H_2SO_4 at room temperature for one day. Under these conditions, the only products formed were 5-amino-1,3,4-thiadiazol-2-yl-substituted imidazole *N*-oxides **6** (*Scheme 2*). Unexpectedly, the reactions carried out under these conditions with **4b** and **4i**, which were derived from phenylisothiocyanate, yielded **6b** and **6e**, respectively, bearing a phenylsulfonic acid residue (R^2 = 4-$HO_3SC_6H_4$). It is very likely that these products result from the sulfonation of the intermediate 5-phenylamino-1,3,4-thiadizole derivatives formed after the initial cyclocondensation step[2]). Based on the comparison of the chemical shifts of *H*–C(2) in **6b** and in the analogous MeN and BuN derivatives **6a** and **6c**, respectively, a zwitterionic structure can be postulated for both arylsulfonic acids **6b** and **6e** (see *Scheme 5*). To the best of our knowledge, secondary sulfonation of 5-phenylamino-1,3,4-thiadiazoles obtained from corresponding thiosemicarbazides in the presence of H_2SO_4 under similar reaction conditions (r.t.) has not been reported so far [12][13].

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[2]) The sulfonation of aniline with conc. H_2SO_4 at elevated temperatures is a well known process [9] and has been studied in detail by *Khelevin* [10]. A study of the thermolysis of diphenylammonium hydrogen sulfate leading to 4-(phenylamino)benzenesulfonic acid has bee published recently [11].

Similarly to the reactions with isothiocyanates, hydrazides **1a** and **1b** reacted with butyl isocyanate in refluxing EtOH yielding semicarbazides **7a** and **7b**, respectively, as crystalline materials in high yields (*Scheme 3*). After isolation and purification, they were used for the synthesis of bis-heterocyclic 1,2,4-triazol-3-ones **8a**,**b** under basic conditions. Both products **7** and **8** were obtained with the preserved *N*-oxide function.

Scheme 3

Transformation of hydrazides into 3-alkyl-1,3,4-oxadiazoles can be performed *via* cyclization of their *N*-acyl derivatives under acidic conditions [5]. In the case of hydrazides **1a** and **1c**, the acetylation performed with a slight excess of Ac_2O in boiling EtOH afforded the expected *N*-acetyl derivatives **9** (*Scheme 4*). Apparently, this conversion is much faster than the alternative isomerization to the corresponding imidazol-2-ones reported as a typical reaction of 2-unsubstituted imidazole *N*-oxides by treatment with Ac_2O [8b]. However, the attempted cyclocondensations of products **9** under acidic conditions (H_2SO_4, r.t.) were unsuccessful.

Scheme 4

In a series of reports we demonstrated that the treatment of 2-unsubstituted imidazole *N*-oxides with a cycloaliphatic thioketone, *e.g.*, 2,2,4,4-tetramethylcyclobutane-1,3-dithione (**10**) opens an easy access to imidazole-2-thiones [8a,c,e,f]. On the other hand, we found recently that the presence of a hydrazide group at C(4) inhibits the S-transfer reaction [6]. Having in hand bis-heterocyclic imdazole *N*-

oxides of type **5** and **6**, the S-transfer with **10** was tested. In both cases (**5g**, **6e**), the desired imidazole-2-thiones were smoothly formed at room temperature (*Scheme 5*).

Scheme 5

This result points out the influence of the intramolecular H-bond on the 'nitrone-like' reactivity of the imidazole *N*-oxides **1**. Whereas the strong H-bond in the hydrazides [6] causes reduced reactivity, there is no such H-bond present in the bis-heterocyclic imidazole *N*-oxides **5** and **6**, which easily enter a [2 + 3] cycloaddition with **10**.

Conclusions. – The present study shows that imidazole carbohydrazides of type **1**, containing the *N*-oxide function, react with isothiocyanates, isocyanates, and Ac_2O in a typical manner yielding the corresponding thiosemicarbazides **4**, semicarbazides **7**, and *N*-acetyl derivatives **9**, respectively, in high yields. In the case of thiosemicarbazides, cyclizations to 1,2,4-triazole-3-thiones **5** and 2-amino-1,3,4-thiadiazoles **6** were performed under basic and acidic conditions, correspondingly. Similarly, semicarbazides **7** were converted into 1,2,4-triazole-3-ones **8** in aqueous NaOH solution. In all these reactions, the *N*-oxide function in the imidazole ring was preserved. However, attempted acid-catalyzed cyclizations of **7** and **9** to the corresponding 3-amino- and 3-methyl-1,3,4-oxadiazoles, respectively, were unsuccessful.

In contrast to hydrazides **1**, which were shown not to undergo the S-transfer reaction upon treatment with the dithione **10** under standard conditions [6], bis-heterocyclic imidazole *N*-oxides of type **5** and **6** smoothly undergo this reaction.

To the best of our knowledge, the elaborated protocol offers a unique route for the synthesis of bis-heterocyclic *N*-oxides, which cannot be prepared using an oxidative approach. This novel type of *N*-oxides may be of interest as a new group of ligands for coordination chemistry. Moreover, in a recent paper, derivatives of 5-amino-1,3,4-thiadiazoles obtained from 5-methylimidazole-4-carbohydrazide according to the general method described in the present paper, displayed high anti-*Toxoplasma gondi* and antimicrobial activities [13].

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Experimental Part

1. General. M.p.: *STUART SMP30*; uncorrected. IR Spectra: *NEXUS FT-IR* spectrophotometer; in KBr; absorptions in cm^{-1}. ^{1}H- and $^{13}C\{^{1}H\}$-NMR Spectra: *Bruker Avance III 600*, in (D_6)DMSO, using solvent signals as reference; δ in ppm; coupling constants *J* in Hz; assignments of signals in ^{13}C-NMR spectra accomplished on the basis of HMQC experiments. HR-ESI-MS: *Finnigan MAT-95;* HR-EI-MS: *Bruker Esquire LC* spectrometer.

2. *Starting Materials*. All solvents are commercially available and used as received. Hydrazides **1a** – **1c** were prepared from the corresponding esters by treatment with $NH_2NH_2 \cdot H_2O$ according to the previously described protocol [6].

3. *Synthesis of Thiosemicarbazides* **4a** – **4j** *and Semicarbazides* **7a** and **7b**. *General Procedure.* A mixture of hydrazide **1** (1 mmol) and the corresponding isothiocyanate (1.1 mmol) or isocyanate (1.1 mmol) in EtOH (5 ml) was heated to reflux for 2 h. Then, the formed product was filtered off, washed with Et_2O and crystallized from MeOH.

*1-{[(1-Benzyl-5-methyl-3-oxido-1*H*-imidazolium-4-yl)carbonyl]amino}-3-methylthiourea* (**4a**) [6].

*1-{[(1-Benzyl-5-methyl-3-oxido-1*H*-imidazolium-4-yl)carbonyl]amino}-3-phenylthiourea* (**4b**): Yield: 0.347 g (91%). Colorless crystals. M.p. 200 – 204° (dec., MeOH). IR (KBr): 3295*s* (NH), 3127*s*, 1663v*s* (C=O), 1599v*s*, 1497*m*, 708*m*. ^{1}H-NMR ((D$_6$)DMSO): 9.80 (br. *s*, NH); 8.72 (*s*, H–C(2')); 7.48 – 7.12 (*m*, 10 arom. H); 5.26 (*s*, CH_2); 2.45 (*s*, Me); two NH absorptions missing. ^{13}C-NMR ((D$_6$)DMSO): 178.2 (C=O); 159.2 (C=S); 139.7, 135.9, 131.2, 121.3 (2 arom. C, C(4'), C(5')); 126.7 (C(2')); 129.5, 128.7, 128.6, 127.7, 127.6, 125.3 (10 arom. CH); 48.7 (CH_2); 9.8 (Me). HR-ESI-MS: 404.1149 ([*M*+Na]$^+$, $C_{19}H_{19}N_5NaO_2S$; calc. 404.1152); 382.1329 ([*M*+H]$^+$, $C_{19}H_{20}N_5O_2S$; calc. 382.1332).

*1-{[(1-Benzyl-5-methyl-3-oxido-1*H*-imidazolium-4-yl)carbonyl]amino}-3-butylthiourea* (**4c**). Yield: 0.343 g (95%). Colorless crystals. M.p. 204 – 207° (MeOH). IR (KBr): 3243*m* (NH), 2955*s*, 1661v*s* (C=O), 1598v*s*, 1552*m*, 1456*m*, 737*m*. ^{1}H-NMR ((D$_6$)DMSO): 12.41, 9.31 (2 br. *s*, 2 NH); 8.72 (*s*, H–C(2')); 8.03 (br. *s*, NH); 7.42 – 7.25 (*m*, 5 arom. H); 5.25 (*s*, CH_2); 3.40 (*q*, *J* = 6.6, CH_2N); 2.43 (*s*, Me); 1.49 – 1.44,

1.28 – 1.22 (2 *m*, 2 CH_2); 0.86 (*t*, *J* = 7.2, Me). ^{13}C-NMR ((D$_6$)DMSO): 181.7 (C=O); 159.6 (C=S); 135.9, 131.2, 121.3 (1 arom. C, C(4'), C(5')); 126.7 (C(2')); 129.5, 128.7, 127.7 (5 arom. CH); 48.7 (Ph*C*H_2); 43.9 (CH_2N); 31.3, 19.9 (2 CH_2); 14.2 (Me); 9.8 (MeC(2')). HR-ESI-MS: 384.1467 ([*M*+Na]$^+$, $C_{17}H_{23}N_5NaO_2S$; calc. 384.1465); 362.1643 ([*M*+H]$^+$, $C_{17}H_{24}N_5O_2S$; calc. 362.1645).

*1-{[(1-Benzyl-5-methyl-3-oxido-1*H*-imidazolium-4-yl)carbonyl]amino}-3-(*tert*-butyl)thiourea* (**4d**). Yield: 0.235 g (65%). Colorless crystals. M.p. 201 – 203° (MeOH). IR (KBr): 3235*m* (NH), 3088*s*, 1668v*s* (C=O), 1599v*s*, 1541*m*, 1362*m*, 709*m*. ^{1}H-NMR ((D$_6$)DMSO): 9.51 (br. *s*, NH); 8.67 (*s*, H–C(2')); 7.41 – 7.25 (*m*, 5 arom. H); 5.24 (*s*, CH_2); 2.43 (*s*, Me); 1.44 (*s*, *Me*$_3$C); two NH absorptions missing. ^{13}C-NMR ((D$_6$)DMSO): 178.9 (C=O); 159.8 (C=S); 135.8, 131.1, 120.9 (1 arom. C, C(4'), C(5')); 126.7 (C(2')); 129.4, 128.6, 127.7 (5 arom. CH); 53.2 (Me$_3$*C*); 48.7 (CH_2); 29.1 (3 *Me*$_3$C); 9.8 (MeC(2')). HR-ESI-MS: 384.1469 ([*M*+Na]$^+$, $C_{17}H_{23}N_5NaO_2S$; calc. 384.1465); 362.1646 ([*M*+H]$^+$, $C_{17}H_{24}N_5O_2S$; calc. 362.1645).

*1-{[(1,5-Dimethyl-3-oxido-1*H*-imidazolium-4-yl)carbonyl]amino}-3-methylthiourea* (**4e**). Yield: 0.173 g (71%). Colorless crystals. M.p. 229 – 231° (MeOH). IR (KBr): 3160*s*, 2974*s*, 1638v*s* (C=O), 1602v*s*, 1485*s*, 1285*m*, 606*m*. ^{1}H-NMR ((D$_6$)DMSO): 9.35 (br. *s*, NH); 8.48 (*s*, H–C(2')); 8.01 (br. *s*, NH); 3.58 (*s*, imidazole Me); 2.85 (*d*, *J* = 4.1, MeN); 2.48 (*s*, Me); one NH absorption missing. ^{13}C-NMR ((D$_6$)DMSO): 182.6 (C=O); 159.8 (C=S); 131.8, 120.7 (C(4'), C(5')); 126.8 (C(2')); 32.4 (MeN(1')); 31.4 (MeN); 9.5 (MeC(2')). HR-ESI-MS: 266.0682 ([*M*+Na]$^+$, $C_8H_{13}N_5NaO_2S$; calc. 266.0682); 244.0859 ([*M*+H]$^+$, $C_8H_{14}N_5O_2S$; calc. 244.0863).

*1-{[(1,5-Dimethyl-3-oxido-1*H*-imidazolium-4-yl)carbonyl]amino}-3-phenylthiourea* (**4f**). Yield: 0.262 g (86%). Colorless crystals. M.p. 223 – 225° (MeOH). IR (KBr): 3245*m* (NH), 3093*s*, 3036*s*, 1667v*s* (C=O), 1600v*s*, 1497*s*, 1321*s*, 760*m*. ^{1}H-

NMR ((D$_6$)DMSO): 9.79 (br. *s*, NH); 8.48 (*s*, H–C(2')); 7.50 – 7.11 (*m*, 5 arom. H); 3.58 (*s*, MeN); 2.50 (*s*, Me; overlaps with DMSO signal); two NH absorptions missing. ^{13}C-NMR ((D$_6$)DMSO): 179.0 (C=O); 160.8 (C=S); 139.8, 131.6, 120.7 (1 arom. C, C(4'), C(5')); 128.8, 128.6, 125.1 (5 arom. CH); 126.8 (C(2')); 32.4 (MeN); 9.5 (MeC(2')). HR-ESI-MS: 328.0835 ([*M*+Na]$^+$, $C_{13}H_{15}N_5NaO_2S$; calc. 328.0839); 306.1013 ([*M*+H]$^+$, $C_{13}H_{16}N_5O_2S$; calc. 306.1019).

*1-{[(1,5-Dimethyl-3-oxido-1*H*-imidazolium-4-yl)carbonyl]amino}-3-butylthiourea* (**4g**). Yield: 0.262 g (92%). Colorless crystals. M.p. 208 – 210° (MeOH). IR (KBr): 3189*s*, 2957*s*, 1640v*s* (C=O), 1599v*s*, 1483*s*, 1277*m*, 616*m*. ^{1}H-NMR ((D$_6$)DMSO): 12.44, 9.30 (2 br. *s*, 2 NH); 8.47 (*s*, H–C(2')); 8.01 (br. *s*, NH); 3.58 (*s*, MeN); 3.40 (*q*, *J* = 6.6, CH_2N); 2.48 (*s*, Me); 1.49 – 1.44, 1.29 – 1.22 (2 *m*, 2 CH_2); 0.87 (*t*, *J* = 7.2, Me). ^{13}C-NMR ((D$_6$)DMSO): 181.7 (C=O); 159.5 (C=S); 131.7, 120.7 (C(4'), C(5')); 126.8 (C(2')); 43.9 (CH_2N); 31.4 (MeN); 31.3, 19.9 (2 CH_2); 14.2 (Me); 9.5 (MeC(2')). HR-ESI-MS: 308.1151 ([*M*+Na]$^+$, $C_{11}H_{19}N_5NaO_2S$; calc. 308.1152); 286.1329 ([*M*+H]$^+$, $C_{11}H_{20}N_5O_2S$; calc. 286.1332).

*1-{[(1-Cyclohexyl-5-methyl-3-oxido-1*H*-imidazolium-4-yl)carbonyl]amino}-3-methylthiourea* (**4h**). Yield: 0.258 g (83%). Colorless crystals. M.p. 207 – 211° (MeOH). IR (KBr): 3250*s* (NH), 3139*s*, 1664v*s* (C=O), 1596v*s*, 1552*m*, 1495*m*, 1259*m*. ^{1}H-NMR ((D$_6$)DMSO): 12.45, 9.35 (2 br. *s*, 2 NH); 8.72 (*s*, H–C(2')); 8.00 (br. *s*, NH); 4.12 – 4.07 (*m*, CH); 2.85 (*d*, *J* = 4.4, MeN); 2.55 (*s*, Me); 1.92 – 1.79 (*m*, 4 cyclohexyl H); 1.67 – 1.60 (*m*, 3 cyclohexyl H); 1.44 – 1.38 (*m*, 2 cyclohexyl H); 1.21 – 1.13 (*m*, 1 cyclohexyl H). ^{13}C-NMR ((D$_6$)DMSO): 182.6 (C=O); 159.9 (C=S); 130.7, 120.3 (C(4'), C(5')); 124.5 (C(2')); 55.1 (CH); 33.0, 25.3, 25.0 (5 cyclohexyl CH_2); 31.4 (MeN); 9.5 (MeC(2')). HR-ESI-MS: 334.1306 ([*M*+Na]$^+$, $C_{13}H_{21}N_5NaO_2S$; calc. 334.1308); 312.1488 ([*M*+H]$^+$, $C_{13}H_{22}N_5O_2S$; calc. 312.1489).

*1-{[(1-Cyclohexyl-5-methyl-3-oxido-1*H*-imidazolium-4-yl)carbonyl]amino}-3-phenylthiourea* (**4i**). Yield: 0.332 g (89%). Colorless crystals. M.p. 174 – 176° (MeOH). IR (KBr): 3231*s* (NH), 3139*s*, 2934*s*, 1675v*s* (C=O), 1600v*s*, 1497*m*, 1257*m*. ^{1}H-NMR ((D$_6$)DMSO): 9.81 (br. *s*, NH); 8.73 (*s*, H–C(2')); 7.50 – 7.12 (*m*, 5 arom. H); 4.12 – 4.07 (*m*, CH); 2.57 (*s*, Me); 1.93 – 1.80 (*m*, 4 cyclohexyl H); 1.67 – 1.61 (*m*, 3 cyclohexyl H); 1.45 – 1.38 (*m*, 2 cyclohexyl H); 1.22 – 1.14 (*m*, 1 cyclohexyl H); two NH absorptions missing. ^{13}C-NMR ((D$_6$)DMSO): 172.4 (C=O); 156.2 (C=S); 139.7, 130.6, 120.3 (1 arom. C, C(4'), C(5')); 129.4, 129.1, 128.6 (5 arom. CH); 124.4 (C(2')); 55.1 (CH); 33.0, 25.4, 25.0 (5 cyclohexyl CH$_2$); 9.5 (MeC(2')). HR-ESI-MS: 396.1469 ([*M*+Na]$^+$, $C_{18}H_{23}N_5NaO_2S$; calc. 396.1465); 374.1649 ([*M*+H]$^+$, $C_{18}H_{24}N_5O_2S$; calc. 374.1645).

*1-{[(1-Cyclohexyl-5-methyl-3-oxido-1*H*-imidazolium-4-yl)carbonyl]amino}-3-butylthiourea* (**4j**). Yield: 0.318 g (90%). Colorless crystals. M.p. 176 – 180° (MeOH). IR (KBr): 3302*s* (NH), 3143*s*, 2934*s*, 1681v*s* (C=O), 1604v*s*, 1545*m*, 1265*m*. ^{1}H-NMR ((D$_6$)DMSO): 12.48, 9.26 (2 br. *s*, 2 NH); 8.72 (*s*, H–C(2')); 8.02 (br. *s*, NH); 4.11 – 4.07 (*m*, CH); 3.43 – 3.38 (*m*, CH$_2$N); 2.55 (*s*, Me); 1.92 – 1.79 (*m*, 4 cyclohexyl H); 1.67 – 1.60 (*m*, 3 cyclohexyl H); 1.49 – 1.38 (*m*, 2 cyclohexyl H, butyl CH$_2$); 1.28 – 1.15 (*m*, 1 cyclohexyl H, butyl CH$_2$); 0.87 (*t*, *J* = 7.6, Me). ^{13}C-NMR ((D$_6$)DMSO): 181.7 (C=O); 159.8 (C=S); 130.6, 120.3 (C(4'), C(5')); 124.4 (C(2')); 55.0 (CH); 43.9 (CH$_2$N); 33.0, 25.3, 25.0 (5 cyclohexyl CH$_2$); 31.3, 19.9 (2 butyl CH$_2$); 14.2 (Me); 9.5 (MeC(2')). HR-ESI-MS: 376.1777 ([*M*+Na]$^+$, $C_{16}H_{27}N_5NaO_2S$; calc. 376.1778); 354.1955 ([*M*+H]$^+$, $C_{16}H_{28}N_5O_2S$; calc. 354.1958).

*1-{[(1-Benzyl-5-methyl-3-oxido-1*H*-imidazolium-4-yl)carbonyl]amino}-3-butylylurea* (**7a**). Yield: 0.338 g (98%). Colorless crystals. M.p. 201 – 205° (MeOH). IR (KBr): 3304*s* (NH), 3105*m*, 2960*m*, 1656v*s* (C=O), 1603*s*, 1544*m*. ^{1}H-NMR

((D_6)DMSO): 12.08 (br. *s*, NH); 8.67 (*s*, H–C(2')); 7.41 – 7.23 (*m*, 5 arom. H); 7.94, 6.42 (2 br. *s*, 2 NH); 5.24 (*s*, CH_2); 3.01 (*q*, *J* = 7.0, CH_2N); 2.42 (*s*, Me); 1.38 – 1.34, 1.29 – 1.22 (2 *m*, 2 CH_2); 0.86 (*t*, *J* = 7.0, Me). ^{13}C-NMR ((D_6)DMSO): 159.5, 158.0 (2 C=O); 135.9, 131.0, 121.3 (1 arom. C, C(4'), C(5')); 126.8 (C(2')); 129.4, 128.6, 127.6 (5 arom. CH); 48.7 (Ph*C*H_2); 39.4 (CH_2N); 32.4, 19.9 (2 CH_2); 14.2 (Me); 9.7 (MeC(2')). HR-ESI-MS: 368.1697 ([*M*+Na]$^+$, $C_{17}H_{23}N_5NaO_3$; calc. 368.1693); 346.1875 ([*M*+H]$^+$, $C_{17}H_{24}N_5O_3$; calc. 346.1874).

*1-{[(1,5-Dimethyl-3-oxido-1*H*-imidazolium-4-yl)carbonyl]amino}-3-butylurea* (**7b**). Yield: 0.256 g (95%). Colorless crystals. M.p. 190 – 193° (MeOH). IR (KBr): 3308v*s*, 3132*m*, 2957*s*, 1644v*s* (C=O), 1602*s*, 1534*s*, 1254*m*, 608*m*. ^{1}H-NMR ((D_6)DMSO): 12.10 (br. *s*, NH); 8.44 (*s*, H–C(2')); 7.93, 6.39 (2 br. *s*, 2 NH); 3.56 (*s*, MeN); 3.00 (*q*, *J* = 5.8, CH_2N); 2.47 (*s*, Me); 1.39 – 1.34, 1.29 – 1.23 (2 *m*, 2 CH_2); 0.87 (*t*, *J* = 7.0, Me). ^{13}C-NMR ((D_6)DMSO): 159.5, 158.0 (2 C=O); 131.4, 120.7 (C(4'), C(5')); 126.8 (C(2')); 39.4 (CH_2N); 32.4 (MeN); 32.3, 19.9 (2 CH_2); 14.2 (Me); 9.4 (MeC(2')). HR-ESI-MS: 292.1383 ([*M*+Na]$^+$, $C_{11}H_{19}N_5NaO_3$; calc. 292.1380); 270.1560 ([*M*+H]$^+$, $C_{11}H_{20}N_5O_3$; calc. 270.1561).

4. *Synthesis of 1,2,4-Triazole-3-thiones* **5**. *General Procedure*. A mixture of thiosemicarbazide **4** (1 mmol) and a 2% aq. soln. of NaOH (5 ml) was heated to reflux for 2 h. Then, the soln. was neutralized with AcOH and the formed precipitate was filtered off and crystallized from MeOH.

*1-Benzyl-4-(4,5-dihydro-4-methyl-5-thioxo-1*H*-1,2,4-triazol-3-yl)-5-methyl-1*H*-imidazole 3-Oxide* (**5a**) [6].

*1-Benzyl-4-(4,5-dihydro-4-phenyl-5-thioxo-1*H*-1,2,4-triazol-3-yl)-5-methyl-1*H*-imidazole 3-Oxide* (**5b**). Yield: 0.192 g (53%). Colorless crystals. M.p. 262 – 264° (dec. MeOH). IR (KBr): 3110*s*, 3044*m*, 1497*s*, 1319*m*, 688*m*. ^{1}H-NMR ((D_6)DMSO): 8.35 (*s*,

H–C(2)); 7.47 – 7.28 (*m*, 10 arom. H); 5.11 (*s*, CH_2N); 1.92 (*s*, Me); NH absorption missing. ^{13}C-NMR ((D$_6$)DMSO): 168.8 (C=S); 141.4 (triazole C(3)); 134.3, 128.8, 136.2, 117.6 (2 arom. C, imidazole C(4), C(5)); 129.3, 129.2, 128.4, 127.7, 127.2, 126.8 (10 arom. CH); 126.2 (imidazole C(2)); 48.8 (CH_2N); 8.9 (Me). HR-ESI-MS: 386.1041 ([*M*+Na]$^+$, $C_{19}H_{17}N_5NaOS$; calc. 386.1046); 364.1221 ([*M*+H]$^+$, $C_{19}H_{18}N_5OS$; calc. 364.1227).

*1-Benzyl-4-(4,5-dihydro-4-butyl-5-thioxo-1*H*-1,2,4-triazol-3-yl)-5-methyl-1*H*-imidazole 3-Oxide* (**5c**). Yield: 0.240 g (70%). Colorless crystals. M.p. 256–258° (MeOH). IR (KBr): 3129*m*, 2930*m*, 1455*m*, 1294*m*, 730*m*. ^{1}H-NMR ((D$_6$)DMSO): 8.60 (*s*, H–C(2)); 7.41 – 7.25 (*m*, 5 arom. H); 5.26 (*s*, CH_2N); 4.12 (*t*, *J* = 6.8, CH_2N); 2.08 (*s*, Me); 1.45 – 1.40 (*m*, CH_2); 1.04 – 0.98 (*m*, CH_2); 0.67 (*t*, *J* = 6.8, Me); NH absorption missing. ^{13}C-NMR ((D$_6$)DMSO): 167.9 (C=S); 141.7 (triazole C(3)); 136.1, 128.4, 118.5 (1 arom. C, imidazole C(4), C(5)); 129.4, 128.6, 127.6 (5 arom. CH); 126.7 (imidazole C(2)); 49.2 (CH_2N); 44.0 (butyl CH_2N); 30.1, 19.4 (2 butyl CH_2); 13.7 (butyl Me); 9.1 (Me). HR-ESI-MS: 366.1359 ([*M*+Na]$^+$, $C_{17}H_{21}N_5NaOS$; calc. 366.1359); 344.1537 ([*M*+H]$^+$, $C_{17}H_{22}N_5OS$; calc. 344.1540).

*1,5-Dimethyl-4-(4,5-dihydro-4-methyl-5-thioxo-1*H*-1,2,4-triazol-3-yl)-1*H*-imidazole 3-Oxide* (**5d**). Yield: 0.144 g (64%). Colorless crystals. M.p. 321 – 323° (MeOH). IR (KBr): 3147v*s* (NH), 1515*m*, 1455*m*, 1329*m*, 929*m*. ^{1}H-NMR ((D$_6$)DMSO): 8.31 (*s*, H–C(2)); 3.58, 3.44 2(*s*, 2 MeN); 2.17 (*s*, Me); NH absorption missing. ^{13}C-NMR ((D$_6$)DMSO): 168.2 (C=S); 142.3 (triazole C(3)); 128.1, 118.7 (imidazole C(4), C(5)); 126.2 (imidazole C(2)); 32.7, 31.4 (2 MeN); 9.1 (Me). HR-ESI-MS: 248.0574 ([*M*+Na]$^+$, $C_8H_{11}N_5NaOS$; calc. 248.0577); 226.0755 ([*M*+H]$^+$, $C_8H_{12}N_5OS$; calc. 226.0757).

*1,5-Dimethyl-4-(4,5-dihydro-4-phenyl-5-thioxo-1*H*-1,2,4-triazol-3-yl)-1*H*-imidazole 3-Oxide* (**5e**). Yield: 0.155 g (54%). Colorless crystals. M.p. 270 – 274° (dec. MeOH). IR (KBr): 3156v*s* (NH), 1506*m*, 1497*s*, 1326*m*, 694*m*. ^{1}H-NMR ((D$_6$)DMSO): 8.14 (*s*, H–C(2)); 7.51 – 7.38 (*m*, 5 arom. H); 3.45 (*s*, MeN); 2.09 (*s*, Me); NH absorption missing. ^{13}C-NMR ((D$_6$)DMSO): 169.0 (C=S); 141.7 (triazole C(3)); 136.9, 128.9, 117.1 (1 arom. C, imidazole C(4), C(5)); 129.4, 129.1, 127.8 (5 arom. CH); 126.2 (imidazole C(2)); 32.6 (MeN); 8.7 (Me). HR-ESI-MS: 310.0733 ([*M*+Na]$^+$, $C_{13}H_{13}N_5NaOS$; calc. 310.0733); 288.0911 ([*M*+H]$^+$, $C_{13}H_{14}N_5OS$; calc. 288.0914).

*1,5-Dimethyl-4-(4-butyl-4,5-dihydro-5-thioxo-1*H*-1,2,4-triazol-3-yl)-1*H*-imidazole 3-Oxide* (**5f**). Yield: 0.143 g (50%). Colorless crystals. M.p. 240 – 242° (MeOH). IR (KBr): 3162*s* (NH), 2953*s*, 1570*m*, 1449*m*, 1348*m*, 1295*m*, 926*m*. ^{1}H-NMR ((D$_6$)DMSO): 8.38 (*s*, H–C(2)); 4.14 (*t*, *J* = 7.7, CH_2N); 3.59 (*s*, MeN); 2.17 (*s*, Me); 1.51 – 1.46, 1.12 – 1.05 (2*m*, 2 CH_2); 0.74 (*t*, *J* = 7.7, Me); NH absorption missing. ^{13}C-NMR ((D$_6$)DMSO): 167.9 (C=S); 142.2 (triazole C(3)); 128.8, 117.5 (imidazole C(4), C(5)); 126.7 (imidazole C(2)); 44.1 (CH_2N); 32.8 (MeN); 30.0, 19.5 (2 CH_2); 13.7, 8.9 (2 Me). HR-ESI-MS: 290.1042 ([*M*+Na]$^+$, $C_{11}H_{17}N_5NaOS$; calc. 290.1046); 268.1225 ([*M*+H]$^+$, $C_{11}H_{18}N_5OS$; calc. 268.1227).

*1-Cyclohexyl-4-(4,5-dihydro-4-methyl-5-thioxo-1*H*-1,2,4-triazol-3-yl)-5-methyl-1*H*-imidazole 3-Oxide* (**5g**). Yield: 0.240 g (82%). Colorless crystals. M.p. 212 – 216° (MeOH). IR (KBr): 3115*s* (NH), 2941*s*, 1559*m*, 1418*m*, 1324*m*. ^{1}H-NMR ((D$_6$)DMSO): 8.49 (*s*, H–C(2)); 4.05 – 4.00 (*m*, CH); 3.42 (*s*, MeN); 2.20 (*s*, Me); 1.97 – 1.80 (*m*, 4 cyclohexyl H); 1.69 – 1.62 (*m*, 3 cyclohexyl H); 1.45 – 1.38 (*m*, 2 cyclohexyl H); 1.23 – 1.14 (*m*, 1 cyclohexyl H); NH absorption missing. ^{13}C-NMR ((D$_6$)DMSO): 168.3 (C=S); 142.1 (triazole C(3)); 126.7, 118.7 (imidazole C(4), C(5)); 123.6 (imidazole C(2)); 55.5 (CH); 33.2 (MeN); 31.4, 25.4, 23.1 (5 cyclohexyl CH_2); 9.2 (Me). HR-ESI-

MS: 316.1200 ([*M*+Na]$^+$, $C_{13}H_{19}N_5NaOS$; calc. 316.1203); 294.1379 ([*M*+H]$^+$, $C_{13}H_{20}N_5OS$; calc. 294.1383).

*1-Cyclohexyl-4-(4,5-dihydro-4-phenyl-5-thioxo-1*H-*1,2,4-triazol-3-yl)-5-methyl-1*H-*imidazole 3-Oxide* (**5h**). Yield: 0.185 g (52%). Colorless crystals. M.p. 282 – 284° (MeOH). IR (KBr): 3231*m* (NH), 2936*m*, 1601*m*, 1497*m*, 1320*m*. ^{1}H-NMR ((D$_6$)DMSO): 8.34 (*s*, H–C(2)); 7.45 – 7.37 (*m*, 5 arom. H); 3.92 – 3.85 (*m*, CH); 2.07 (*s*, Me); 1.79 – 1.74 (*m*, 4 cyclohexyl H); 1.62 – 1.49 (*m*, 3 cyclohexyl H); 1.37 – 1.30 (*m*, 2 cyclohexyl H); 1.15 – 1.12 (*m*, 1 cyclohexyl H); NH absorption missing. ^{13}C-NMR ((D$_6$)DMSO): 168.9 (C=S); 141.6 (triazole C(3)); 134.1, 126.1, 118.4 (1 arom. C, imidazole C(4), C(5)); 129.3, 129.0, 127.7 (5 arom. CH); 123.6 (imidazole C(2)); 55.4 (CH); 33.0, 25.3, 24.9 (5 cyclohexyl CH$_2$); 8.9 (Me). HR-ESI-MS: 378.1361 ([*M*+Na]$^+$, $C_{18}H_{21}N_5NaOS$; calc. 378.1359); 356.1541 ([*M*+H]$^+$, $C_{18}H_{22}N_5OS$; calc. 356.1540).

*1-Cyclohexyl-4-(4-butyl-4,5-dihydro-5-thioxo-1*H-*1,2,4-triazol-3-yl)-5-methyl-1*H-*imidazole 3-Oxide* (**5i**). Yield: 0.251 g (75%). Colorless crystals. M.p. 248–250° (MeOH). IR (KBr): 3066*m*, 2936*m*, 1356*m*, 1295*m*. ^{1}H-NMR ((D$_6$)DMSO): 8.55 (*s*, H–C(2)); 4.12 (*t*, *J* = 6.8, CH$_2$N); 4.07 – 4.02 (*m*, CH); 2.20 (*s*, Me); 1.95 – 1.81 (*m*, 4 cyclohexyl H); 1.69 – 1.62 (*m*, 3 cyclohexyl H); 1.48 – 1.38 (*m*, 2 cyclohexyl H, butyl CH$_2$); 1.22 – 1.17 (*m*, 1 cyclohexyl H); 1.07 – 1.01 (*m*, butyl CH$_2$); 0.69 (*t*, *J* = 6.8, Me); NH absorption missing. ^{13}C-NMR ((D$_6$)DMSO): 167.9 (C=S); 141.9 (triazole C(3)); 123.1, 118.4 (imidazole C(4), C(5)); 123.9 (imidazole C(2)); 55.6 (CH); 43.7 (CH$_2$N); 33.2, 25.4, 25.0 (5 cyclohexyl CH$_2$); 30.0, 19.3 (2 butyl CH$_2$); 13.6, 9.0 (2 Me). HR-HR-ESI-MS: 358.1677 ([*M*+Na]$^+$, $C_{16}H_{25}N_5NaOS$; calc. 358.1672); 336.1856 ([*M*+H]$^+$, $C_{16}H_{26}N_5OS$; calc. 336.1853).

5. *Synthesis of 1,3,4-Thiadiazoles* **6**. *General procedure*. A soln. of thiosemicarbazide **4** (1 mmol) in conc. H_2SO_4 (5 ml) was kept at r.t. for 1 d. After

neutralization of the soln. with diluted NH_4OH, the solid product was filtered off, dried, and crystallized from MeOH.

*1-Benzyl-5-methyl-4-(5-methylamino-1,3,4-thiadiazol-2-yl)-1*H-*imidazole 3-Oxide* (**6a**) [6].

*1-Benzyl-5-methyl-4-[5-(4-sulfophenyl)amino]-1,3,4-thiadiazol-2-yl)-1*H-*imidazole 3-Oxide* (**6b**). Yield: 0.211 g (58%). Yellowish crystals. M.p. 300 – 303° (dec., MeOH). IR (KBr): 3400–2800*m* (br), 3124*m*, 3064*m*, 1509*s*, 1176*m* (br), 1034*m*, 708*m*. ^{1}H-NMR ((D$_6$)DMSO): 10.34 (br. *s*, NH); 8.66 (*s*, H–C(2)); 7.60, 7.57 (*AA'BB'* , J_{AB} = 8.4, 4 arom. H); 7.42 – 7.28 (*m*, 5 arom. H); 5.29 (*s*, CH_2); 2.56 (*s*, Me). ^{13}C-NMR ((D$_6$)DMSO): 164.4, 146.4 (thiadiazole C(2), C(5)); 142.1, 141.4, 136.1, 122.7, 116.6 (3 arom. C, imidazole C(4), C(5)); 129.4, 128.6, 127.7, 127.0, 125.0 (9 arom. CH); 125.6 (imidazole C(2)); 49.0 (CH_2); 10.2 (Me). HR-ESI-MS: 488.0432 ([*M*–1+2 Na]$^+$, $C_{19}H_{16}N_5Na_2O_4S_2$; calc. 488.0434); 466.0610 ([*M*+Na]$^+$, $C_{19}H_{17}N_5NaO_4S_2$; calc. 466.0614); 444.0791 ([*M*+H]$^+$, $C_{19}H_{18}N_5O_4S_2$; calc. 444.0795).

*1-Benzyl-5-methyl-4-(5-butylamino-1,3,4-thiadiazol-2-yl)-1*H-*imidazole 3-Oxide* (**6c**). Yield: 0.209 g (61%). Yellowish crystals. M.p. 206 – 208° (dec., MeOH). IR (KBr): 3185*m*, 3068*m*, 2958*s*, 1576*s*, 1454*m*, 748*m*. ^{1}H-NMR ((D$_6$)DMSO): 8.57 (*s*, H–C(2)); 7.58 (br. *s*, NH); 7.41 – 7.26 (*m*, 5 arom. H); 5.24 (*s*, PhC*H*$_2$); 3.34 – 3.23 (*m*, CH_2N); 2.49 (*s*, Me); 1.59 – 1.54 (*m*, CH_2); 1.39 – 1.33 (*m*, CH_2); 0.90 (*t*, *J* = 7.6, Me). ^{13}C-NMR ((D$_6$)DMSO): 169.2, 144.4 (thiadiazole C(2), C(5)); 136.3, 124.0, 123.0 (1 arom. C, imidazole C(4), C(5)); 129.4, 128.5, 127.6 (5 arom. CH); 125.3 (imidazole C(2)); 48.9 (Ph*C*H$_2$); 44.9 (CH_2N); 31.2, 20.1 (2 CH_2); 14.1, 10.1 (2 Me). HR-ESI-MS: 366.1361 ([*M*+Na]$^+$, $C_{17}H_{21}N_5NaOS$; calc. 366.1359); 344.1541 ([*M*+H]$^+$, $C_{17}H_{22}N_5OS$; calc. 344.1540).

*1,5-Dimethyl-4-(5-methylamino-1,3,4-thiadiazol-2-yl)-1*H-*imidazole 3-Oxide* (**6d**). Yield: 0.207 g (92%). Yellowish crystals. M.p. 228 – 230° (dec., MeOH). IR (KBr): 3375*s* (NH), 3120*s*, 2941*s*, 1541*m*, 1404*m*, 1097*m*, 1033*m*, 604*m*. ^{1}H-NMR ((D$_6$)DMSO): 8.37 (*s*, H–C(2)); 7.55 (br. *s*, NH); 3.59 (*s*, imidazole MeN); 2.89 (br. *s*, MeN); 2.54 (*s*, Me). ^{13}C-NMR ((D$_6$)DMSO): 169.8, 144.8 (thiadiazole C(2), C(5)); 125.4 (imidazole C(2)); 124.5, 122.3 (imidazole C(4), C(5)); 32.5, 31.6 (2 MeN); 9.8 (Me). HR-ESI-MS: 248.0578 ([*M*+Na]$^+$, $C_8H_{11}N_5NaOS$; calc. 248.0577); 226.0760 ([*M*+H]$^+$, $C_8H_{12}N_5OS$; calc. 226.0757).

*1-Cyclohexyl-5-methyl-4-[5-(4-sulfophenyl)amino]-1,3,4-thiadiazol-2-yl)-1*H-*imidazole 3-Oxide* (**6e**). Yield: 0.249 g (70%). Colorless crystals. M.p. 310 – 312° (dec., MeOH). IR (KBr): 3400–2650*m* (br), 3385*s* (NH), 3227*s*, 3038*s*, 1420*s* (br), 1090*s* (br), 613*m*. ^{1}H-NMR ((D$_6$)DMSO): 10.29 (br. *s*, NH); 8.65 (*s*, H–C(2)); 7.60, 7.56 (*AA'BB'*, J_{AB} = 8.4, 4 arom. H); 4.14 – 4.09 (*m*, CH); 2.68 (*s*, Me); 1.99 – 1.81 (*m*, 4 cyclohexyl H); 1.68 – 1.63 (*m*, 3 cyclohexyl H); 1.47 – 1.41 (*m*, 2 cyclohexyl H); 1.24 – 1.21 (*m*, 1 cyclohexyl H). ^{13}C-NMR ((D$_6$)DMSO): 164.4, 146.7 (thiadiazole C(2), C(5)); 142.2, 116.6 (2 arom. C); 141.4, 127.0 (4 arom. CH); 124.2 (imidazole C(2)); 123.1, 121.6 (imidazole C(4), C(5)); 55.3 (CH); 33.1, 25.4, 25.0 (5 cyclohexyl CH$_2$); 9.9 (Me). HR-ESI-MS: 458.0926 ([*M*+Na]$^+$, $C_{18}H_{21}N_5NaO_4S_2$; calc. 458.0927); 436.1110 ([*M*+H]$^+$, $C_{18}H_{22}N_5O_4S_2$; calc. 436.1108).

6. *Synthesis of 1,2,4-Triazole-3-ones* **8**. *General procedure.* A mixture of semicarbazide **7** (1 mmol) and a 2% aq. soln. of NaOH (5 ml) was heated to reflux for 8 h. Then, the soln. was neutralized with AcOH, the formed precipitate was filtered off, and crystallized from MeOH.

*1-Benzyl-4-(4-butyl-4,5-dihydro-5-oxo-1*H-*1,2,4-triazol-3-yl)-5-methyl-1*H-*imidazole 3-Oxide* (**8a**). Yield: 0.216 g (66%). Colorless crystals. M.p. 224 – 228°

(MeOH). IR (KBr): 3115*m*, 2938*m*, 1705v*s* (C=O), 1558*m*, 1416*m*, 734*m*. ^{1}H-NMR ((D$_6$)DMSO): 8.55 (*s*, H–C(2)); 7.41 – 7.24 (*m*, 5 arom. H); 5.23 (*s*, Ph*C*H$_2$); 3.73 (*t*, *J* = 6.8, CH$_2$N); 2.08 (*s*, Me); 1.58 (br. *s*, NH); 1.37 – 1.32, 1.06 – 1.00 (2*m*, 2 CH$_2$); 0.68 (*t*, *J* = 7.7, Me). ^{13}C-NMR ((D$_6$)DMSO): 155.4 (C=O); 137.4, 136.3, 127.8, 119.8 (1 arom. C, imidazole C(4), C(5), triazole C(3)); 129.4, 128.6, 127.6 (5 arom. CH); 126.3 (imidazole C(2)); 49.1 (Ph*C*H$_2$); 41.0 (CH$_2$N); 30.7, 19.4 (2 CH$_2$); 13.6, 9.1 (2 Me). HR-ESI-MS: 350.1589 ([*M*+Na]$^+$, C$_{17}$H$_{21}$N$_5$NaO$_2$; calc. 350.1588), 328.1771 ([*M*+H]$^+$, C$_{17}$H$_{22}$N$_5$O$_2$; calc. 328.1768).

*4-(4-Butyl-4,5-dihydro-5-oxo-1*H*-1,2,4-triazol-3-yl)-1,5-dimethyl-1*H*-imidazole 3-Oxide* (**8b**). Yield: 0.176 g (70%). Colorless crystals. M.p. 214 – 216° (MeOH). IR (KBr): 3409v*s* (NH), 1698v*s* (C=O), 1559v*s*, 1410*s*, 649*m*. ^{1}H-NMR ((D$_6$)DMSO): 8.33 (*s*, H–C(2)); 3.71 (*q*, *J* = 7.0, CH$_2$N); 3.58 (*s*, MeN); 2.16 (*s*, Me); 1.64 (br. *s*, NH); 1.39 – 1.35, 1.10 – 1.06 (2*m*, 2 CH$_2$); 0.74 (*t*, *J* = 7.4, Me). ^{13}C-NMR ((D$_6$)DMSO): 155.6 (C=O); 137.4, 128.2, 118.8 (imidazole C(4), C(5), triazole C(3)); 126.4 (imidazole C(2)); 41.1 (CH$_2$N); 32.7 (MeN); 32.7, 19.5 (2 CH$_2$); 13.7, 8.9 (2 Me). HR-ESI-MS: 290.1012 ([*M*+K]$^+$, C$_{11}$H$_{17}$KN$_5$O$_2$; calc. 290.1014), 274.1273 ([*M*+Na]$^+$, C$_{11}$H$_{17}$N$_5$NaO$_2$; calc. 274.1275), 252.1451 ([*M*+H]$^+$, C$_{11}$H$_{18}$N$_5$O$_2$; calc. 252.1455).

7. *Synthesis of* N-*Acetylhydrazides* **9**. *General procedure*. A mixture of hydrazide **1** (1 mmol) and Ac$_2$O (1.1 mmol) in EtOH (5 ml) was heated to reflux for 2 h. The formed product was then filtered off, washed with Et$_2$O, and crystallized from MeOH.

N'-*Acetyl-1-benzyl-5-methyl-3-oxido-1*H-*imidazolium-4-carbohydrazide* (**9a**). Yield: 1.251 g (87%). Colorless crystals. M.p. 164 − 166° (MeOH). IR (KBr): 3119*s*, 1663v*s* (C=O), 1601v*s*, 1497*m*, 709*m*. ^{1}H-NMR ((D$_6$)DMSO): 12.65, 10.26 (2 br. *s*, 2 NH); 8.68 (*s*, H−C(2)); 7.41 − 7.23 (*m*, 5 arom. H); 5.24 (*s*, CH$_2$); 2.42, 1.90 (2*s*, 2 Me).

^{13}C-NMR ((D$_6$)DMSO): 167.3, 159.7 (2 C=O); 135.6, 131.2, 120.8 (1 arom. C, C(4), C(5)); 129.5, 128.6, 127.6 (5 arom. CH); 126.9 (C(2)); 48.7 (CH_2); 20.9, 9.6 (2 Me). HR-ESI-MS: 311.1118 ([*M*+Na]$^+$, $C_{14}H_{16}N_4NaO_3$; calc. 311.1115); 289.1297 ([*M*+H]$^+$, $C_{14}H_{17}N_4O_3$; calc. 289.1295).

N'-*Acetyl-1-cyclohexyl-5-methyl-3-oxido-1*H-*imidazolium-4-carbohydrazide* (**9b**): Yield: 0.246 g (88%). Colorless crystals. M.p. 184−188° (MeOH). IR (KBr): 3247*s* (NH), 2937*s*, 1654v*s* (C=O), 1601v*s*, 1418*m*, 1047*m*. ^{1}H-NMR ((D$_6$)DMSO): 12.61 (br. *s*, NH); 8.68 (*s*, H−C(2)); 4.10–4.03 (*m*, CH); 2.55 (*s*, Me); 1.93–1.78 (*m*, 4 cyclohexyl H, Me); 1.66–1.59 (*m*, 3 cyclohexyl H); 1.43–1.36 (*m*, 2 cyclohexyl H); 1.20–1.13 (*m*, 1 cyclohexyl H). ^{13}C-NMR ((D$_6$)DMSO): 168.6, 158.0 (2 C=O); 130.7, 119.8 (C(4), C(5)); 124.5 (C(2)); 55.1 (CH); 33.0, 25.3, 24.9 (5 cyclohexyl CH_2); 20.9, 9.4 (2 Me). HR-ESI-MS: 303.14267 ([*M*+Na]$^+$, $C_{13}H_{20}N_4NaO_3$; calc. 303.1428); 281.1607 ([*M*+H]$^+$, $C_{13}H_{21}N_4O_3$; calc. 281.1608).

8. *Synthesis of 1*H-*Imidazole-2-thiones* **11**. *General Procedure*. To a magnetically stirred soln. of 1*H*-imidazole N-oxide **5g** or **6e** (1 mmol) in CH_2Cl_2 (1 ml), a soln. of 2,2,4,4-tetramethylcyclobutane-1,3-dithione (**10**, 0.6 mmol) in CH_2Cl_2 (1 ml) was added dropwise. The addition was complete after *ca.* 10 min, and stirring was continued for 48 h, while a precipitate was formed. Then, the solvent was removed under reduced pressure, the resulting solid was washed with hexane, and filtered. The crude product was recrystallized from MeOH.

*1-Cyclohexyl-4-(4,5-dihydro-4-methyl-5-thioxo-1*H-*1,2,4-triazol-3-yl)-5-methyl-1*H-*imidazole-2(3*H*)-thione* (**11a**). Yield: 0.250 g (81%). Colorless crystals. M.p. 276 – 278° (MeOH). IR (KBr): 3092*s*, 2935*s*, 1560*m*, 1500*m*, 1416*m*, 1348*m*. ^{1}H-NMR ((D$_6$)DMSO): 3.72 (*s*, MeN); 3.35 – 3.29 (*m*, CH); 2.33 (*s*, Me); 1.83 – 1.64 (*m*, 6 cyclohexyl H); 1.36 – 1.16 (*m*, 4 cyclohexyl H); NH absorption missing. ^{13}C-NMR

((D$_6$)DMSO): 171.6, 163.2 (2 C=S); 141.2 (triazole C(3)); 126.3, 116.5 (imidazole C(4), C(5)); 55.4 (CH); 31.7 (MeN); 26.3, 25.8, 21.9 (5 cyclohexyl CH_2); 11.9 (Me). HR-ESI-MS: 332.0973 ([*M*+Na]$^+$, $C_{13}H_{19}N_5NaS_2$; calc. 332.0974), 310.1150 ([*M*+H]$^+$, $C_{13}H_{20}N_5S_2$; calc. 310.1155).

*1-Cyclohexyl-5-methyl-4-[5-(4-sulfophenyl)amino]-1,3,4-thiadiazol-2-yl)-1*H-*imidazole-2(3*H*)-thione* (**11b**). Yield: 0.338 g (91%). Colorless crystals. M.p. 314 – 316° (dec., MeOH). IR (KBr): 3400–2700*m* (br), 3178*s*, 2935*s*, 1405*s* (br), 1122*s* (br), 616*m*. ^{1}H-NMR ((D$_6$)DMSO): 7.57 (br. *s*, 4 arom. H); 3.36 – 3.29 (*m*, CH); 2.57 (*s*, Me); 1.94 – 1.63 (*m*, 6 cyclohexyl H); 1.37 – 1.21 (*m*, 4 cyclohexyl H); NH absorption missing. ^{13}C-NMR ((D$_6$)DMSO): 163.9, 147.3 (thiadiazole C(2), C(5)); 162.9 (C=S); 142.9, 123.0, 120.2, 116.8 (2 arom. C, imidazole C(4), C(5)); 140.1, 127.1 (4 arom. CH); 57.1 (CH); 26.3, 25.3, 21.2 (5 cyclohexyl CH_2); 11.9 (Me). HR-ESI-MS: 474.0695 ([*M*+Na]$^+$, $C_{18}H_{21}N_5NaO_3S_3$; calc. 474.0699), 452.0877 ([*M*+H]$^+$, $C_{18}H_{22}N_5O_3S_3$; calc. 452.0879).

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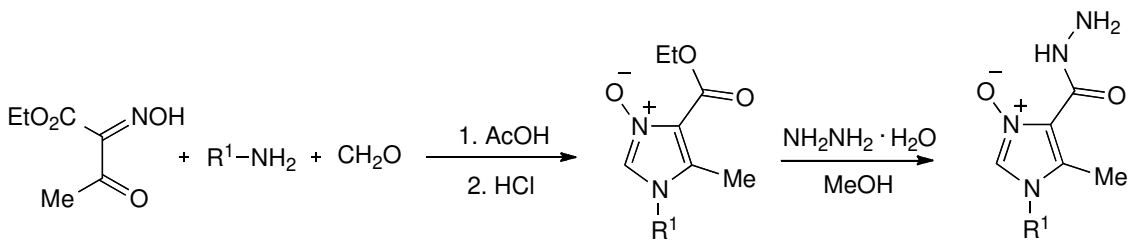
Scheme 1

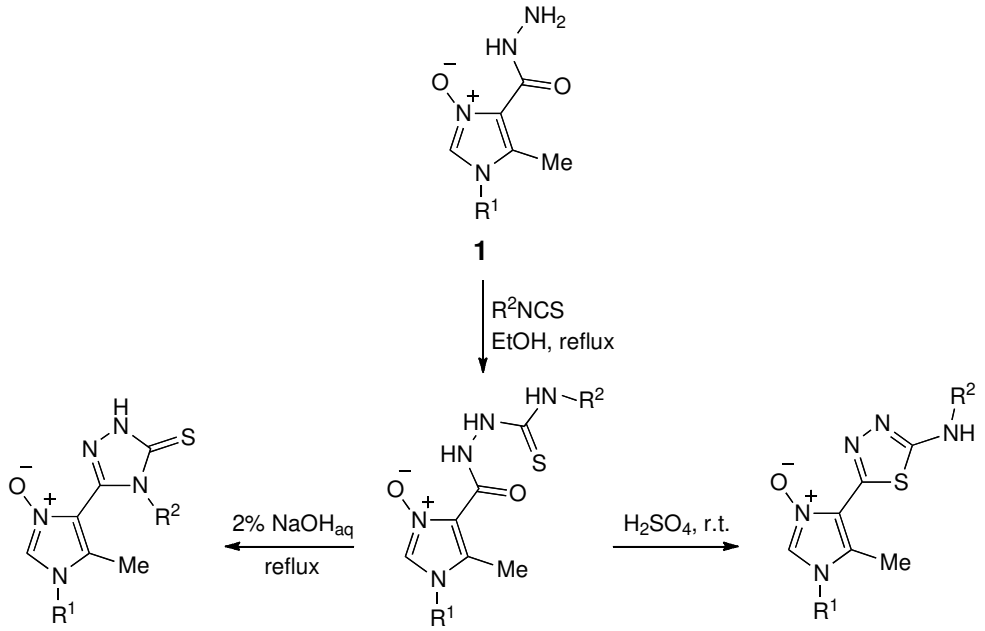


3

2a R^1 = Bn
b R^1 = Me
c R^1 = *c*Hex

1a R^1 = Bn
b R^1 = Me
c R^1 = *c*Hex

Scheme 2

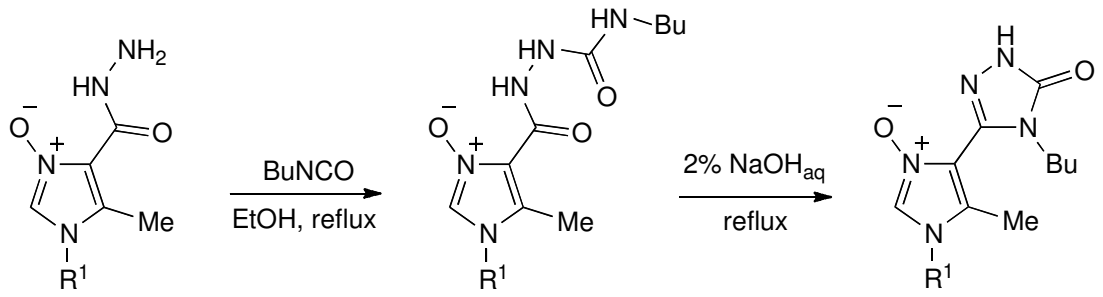


5a R^1 = Bn, R^2 = Me
b R^1 = Bn, R^2 = Ph
c R^1 = Bn, R^2 = Bu
d R^1 = Me, R^2 = Me
e R^1 = Me, R^2 = Ph
f R^1 = Me, R^2 = Bu
g R^1 = *c*Hex, R^2 = Me
h R^1 = *c*Hex, R^2 = Ph
i R^1 = *c*Hex, R^2 = Bu

4a R^1 = Bn, R^2 = Me
b R^1 = Bn, R^2 = Ph
c R^1 = Bn, R^2 = Bu
d R^1 = Bn, R^2 = *t*Bu
e R^1 = Me, R^2 = Me
f R^1 = Me, R^2 = Ph
g R^1 = Me, R^2 = Bu
h R^1 = *c*Hex, R^2 = Me
i R^1 = *c*Hex, R^2 = Ph
j R^1 = *c*Hex, R^2 = Bu

6a R^1 = Bn, R^2 = Me
b R^1 = Bn, R^2 = 4-$HO_3SC_6H_4$
c R^1 = Bn, R^2 = Bu
d R^1 = Me, R^2 = Me
e R^1 = *c*Hex, R^2 = 4-$HO_3SC_6H_4$

Scheme 3

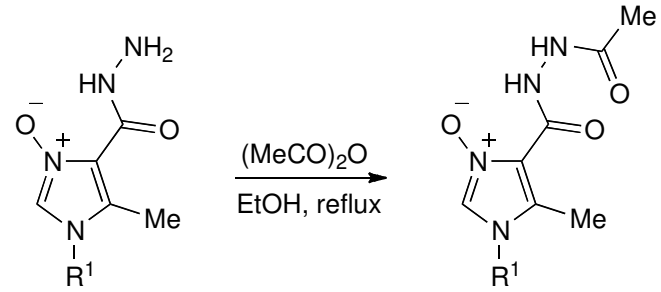


1a R^1 = Bn
b R^1 = Me

7a R^1 = Bn
b R^1 = Me

8a R^1 = Bn
b R^1 = Me

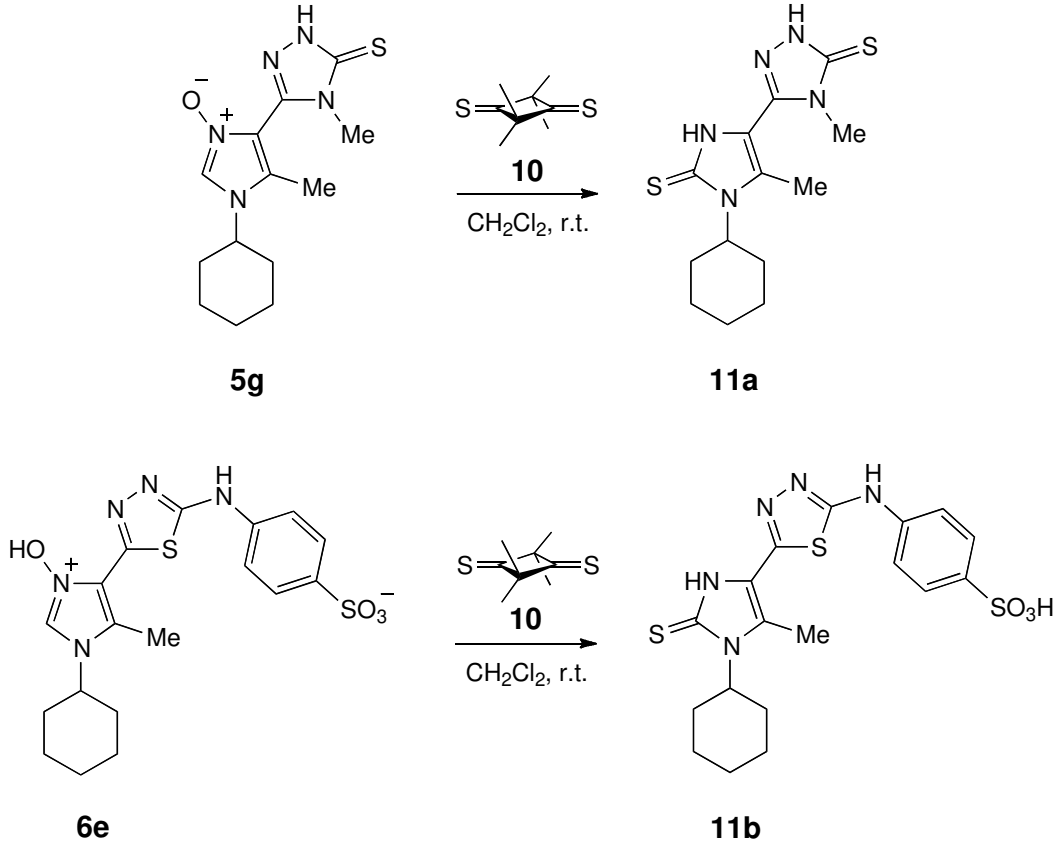
Scheme 4



1a R^1 = Bn
c R^1 = *c*Hex

9a R^1 = Bn
b R^1 = *c*Hex

Scheme 5



Graphical Abstract